IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.:	09/912,031	Confirmation No. 4750
Applicant:	David Cook	
Filed:	July 23, 2001	
TC/A.U.:	1651	
Examiner:	Francisco Prats	
Entitled:	**METHODS FOR QUENCHING PATHOGEN INACTIVATORS IN BIOLOGICAL MATERIALS**	

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Date: September 4, 2003

Linda Aston

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR § 1.78(C)

Dear Sir:

I, David Cook, do depose, declare and state that:

1. I am an inventor of U.S. Patent No. 6,093,725, which was cited by the Examiner in the above-identified patent application.
2. The above-identified application and U.S. Patent No. 6,093,725 are both assigned to Cerus Corporation.
3. I am familiar with contents of the above-identified patent application and the claimed invention in U.S. 6,093,725 were both subject to an obligation of assignment to Cerus Corporation at the time the later invention was made.
4. I am familiar with the contents and claims of the above-identified patent application and the contents and claims of U.S. 6,093,725.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title

18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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Linda Aston

DECLARATION OF SUSAN WOLLOWITZ, Ph.D. UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Susan Wollowitz, hereby declare as follows:

1. I am presently employed by Cerus Corporation, in the position of Vice President of Shared Sciences. I received a Ph.D. in Organic Chemistry in 1980 from the University of Wisconsin-Madison. A copy of my curriculum vitae, describing my background and qualifications, is attached to this Declaration as Exhibit 1.

2. I am not an inventor in the above-identified patent application.

3. I have read and understood the above-identified patent application, the pending claims, the Office Action mailed on May 5, 2003, and the Platz reference, US Patent 5,418,130, cited in the Office Action.

4. The patent application describes the quenching of pathogen inactivation compounds, wherein the compounds act by covalently binding to nucleic acid via the reaction of the electrophilic group of the pathogen inactivation compound and a nucleophilic group of the nucleic acid. The quencher also acts as a nucleophile that reacts

directly with the pathogen inactivation compound. The pathogen inactivation is designed to target nucleic acid via a nucleic acid binding ligand such that sufficient pathogen inactivation compound reacts with pathogen nucleic acid while compound that is not associated with nucleic acid is substantially quenched to avoid unwanted side reactions. The methods and compounds described by Platz do not encompass the methods and compounds of Claim 1.

The preferred embodiment of Platz comprises the following structural features:

- A halogenated psoralen
- A protonated or quarternary amine or phosphine which can also be called a cationic center. This cationic center could bond electrostatically, but would not be reactive as an electrophilic group as it is described in the above-identified application. The amine or phosphine has substituents R', R'' and R''' which are all H or alkyl.
- Platz also discloses the above compounds that contain an ester group between the psoralen and the cation.

The compounds described by the Applicant in Claim 1 have the following structural features:

- A nucleic acid binding moiety (which may be a lipophilic moiety such as a psoralen, e.g. Claim 7).
- A functional group which is, or which forms, an electrophilic group, wherein the electrophilic group can react covalently with the nucleic acid.
- A frangible linker (which may be an ester, Claim 18).

The feature of the functional groups of the two sets, the reactive electrophile of Applicant's claim and the cationic group of Platz, are different. In either case, this group can be an amine.

- The amine (or phosphine) of Platz, however, without other functional groups attached, is not inherently electrophilic, but is generally nucleophilic. Platz does not indicate any functional groups that might alter the nucleophilic nature of such compounds.

A quaternized or protonated amine or phosphine as shown in Platz can interact electrostatically with negatively charged materials but are not known to form covalent bonds.

Nor are they known to form an electrophilic group that can react covalently with nucleic acid without transforming the molecule by chemical reactions that would not occur naturally in the biological medium. The groups that are attached to the amine or phosphine indicated in Platz are hydrogen or linear or branched alkyl groups. These groups are not known to induce an amine or phosphine group to become electrophilic and react covalently with nucleic acids. Likewise, the groups that attach the amine or phosphine to the rest of the molecule are not known to induce them to become electrophilic and react covalently with nucleic acids.

Further, there are no other moieties on the compounds described by Platz that are, or form, electrophilic groups that react covalently with nucleic acids. Platz implies that covalent reaction is not the mechanism of action in his preferred embodiment. Psoralens are known to react with nucleic acids by [2+2] cycloadditions that are distinct from electrophilic reactions [see Song et al., Photochemistry and Photobiology, 29: 1177-1197, 1979, copy enclosed]. Platz suggests, in addition, that his preferred compounds do not react covalently at all with nucleic acids by any means, but rather act via a photochemical route in which the psoralens create free radicals that damage the nucleic acid.

5. One of skill in the art, reading Platz, would not use additives to reduce the production of deleterious species during the decontamination process. The quenching, by additives, of singlet oxygen or highly reactive oxygen species generated from other radiation sensitizers is discussed and considered deleterious to a method of decontaminating a biological composition. "...the sensitizer according to the present invention may be activated at wavelengths and intensities which should reduce the production of singlet oxygen or other highly reactive oxygen species. Thus it is a particular advantage of the present invention to be able to eliminate the use of additives such as ascorbate, sodium thionite, and the like..." (column 8, lines 56-64).

6. The quenching of electrophiles by glutathione as it applies to Applicant's invention is neither described nor implied by Platz. Glutathione, and thiols in general, are known to react with electrophiles by a different mechanism than they react with singlet oxygen or reactive oxidative species. For example, the reaction of nucleophilic glutathione with electrophilic nucleic acid alkylators to protect cells occurs by a process in which the thiol group (RS-) covalently reacts with the alkylator [see, e.g. Bolton et al.,

Drug Metabolism and Disposition 21(6): 986-996, 1993]. The reaction of glutathione with singlet oxygen, other highly reactive oxygen species or free radicals involves the donation of an electron and/or a hydrogen atom to "quench" the reactive species, resulting in the formation of a thiol radical ($RS^{\cdot}$) which can then dimerize, be oxidized further or pull a hydrogen off another thiol in the medium. There is nothing in the disclosure of Platz to suggest that the reactivity of glutathione with an electrophilic nucleic acid alkylator is envisioned.

I declare that all statements made herein based on my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: September 4, 2003

Susan Wollowitz

Susan Wollowitz, Ph.D.